noacetanilide, m.p. 164–165° (lit.,[20] 167–168°); total yield 21%, based on sodium azide.

Phenanthridone from Fluorenone: A. With Trichloroacetic Acid.—On treatment with the same quantities of reagents under the same conditions as described above for β-acetonaphthone, 1.80 g. of fluorenone yielded 1.08 g. (56%) of crude phenanthridone; m.p. *ca.* 220° with sublimation, and 0.86 g. (48%) of crude recovered fluorenone.

B. With Sulfuric Acid.[21]—To a solution of 1.80 g. of fluorenone in 20 cc. of concd. sulfuric acid at room temperature was added with stirring 1.0 g. of sodium azide in portions over half an hour. The mixture was then poured on ice, and the precipitated phenanthridone was filtered off and washed with water and petroleum ether; wt. 1.93 g. (99%), m.p. 290–293° with sublimation (lit.,[22] 293°).

Methyl Azide and Acetophenone.—Solutions of methyl azide in petroleum ether or chloroform were prepared from methyl sulfate and 3.25 g. of sodium azide, according to the method of Dimroth and Wislicenus[23]; the methyl azide was passed in the gas phase through a long tube of soda-lime and potassium hydroxide pellets to remove completely any trace of hydrogen azide. The purity of the product so obtained was confirmed by testing liberal portions with alcoholic silver nitrate and with ferric chloride solution; no opalescence of silver azide was obtained with the first reagent, and no color developed with the second. Mixtures of the methyl azide solutions with 5 cc. of acetophenone and 10 cc. of concd. sulfuric acid foamed vigorously at room temperature. When the reaction subsided, the mixture was poured on ice, and the organic material extracted with ether and steam-distilled. Treatment of the residue in the still-pot with bromine water gave 0.1 to 0.28 g. of *p*-bromoacetanilide in different runs (0.9–2.6%), m.p. 166–168° (lit.,[23] 168°). In an experiment in which aluminum chloride in nitrobenzene was used in place of sulfuric acid, nitrogen evolution was vigorous, but only resinous products were isolated.

Homodihydrocarbostyryl from α-Tetralone.—A mixture of 1.46 g. (0.01 mole) of α-tetralone, 15 g. of trichloroacetic acid, and 1.0 g. (0.015 mole) of sodium azide was heated at 60° for six hours. Pouring the mixture into *ca.* 75 cc. of cold water deposited a brownish, crystalline solid; wt. 2.75 g. (85%), m.p. 109–113°, after washing with water and petroleum ether. Recrystallization from benzene gave an analytical sample; rectangular prisms, m.p. 126°, insol. water and petroleum ether, sol. other organic solvents.

Anal.[24] Calcd. for $C_{10}H_{11}ON \cdot Cl_3CCOOH$: C, 44.45; H, 3.70; Cl, 32.85. Found: C, 44.61; H, 3.88; Cl, 32.67.

This substance could be titrated sharply to a methyl orange end-point, and then left as residue pure homodihydrocarbostyryl, m.p. 139–141° (lit.,[14] 141°), with only mechanical losses. The same addition product was produced at room temperature when equimolar amounts of the components were mixed in concentrated benzene solution.

An attempt to prepare this addition product from α-tetralone oxime by causing it to rearrange in trichloroacetic acid at 60° produced only α-tetralone oxime trichloroacetate, silky needles m.p. 113–115°, insol. water and petroleum ether, sol. other organic solvents. Titration with sodium hydroxide to a methyl orange end-point gave an equivalent weight of 323 (calcd. 324.5) and regenerated α-tetralone oxime, m.p. 101–102° (lit.,[25] 102.5–103.5°), with only mechanical losses.

(20) H. Hübner, *Ann.*, **209**, 355 (1881).
(21) See footnote *l* in table.
(22) C. Graebe and C. A. Wander, *Ann.*, **276**, 248 (1893).
(23) O. Dimroth and W. Wislicenus, *Ber.*, **38**, 1573 (1905).

Summary

1. A qualitative study of the effect of solvents and catalysts on the Schmidt reaction has been made.

2. The occurrence of the Schmidt reaction appears to be governed by the acidity of the medium as determined by the acid strength of the catalyst and the basic strength of the solvent, and by the basic strength of the carbonyl compound undergoing the reaction.

3. Some improvements in carrying out the Schmidt reaction are suggested.

4. The factors influencing the Schmidt reaction are correlated with a carbonium ion mechanism.

(24) Microanalysis by Micro-Tech. Laboratories, Skokie, Illinois.
(25) F. S. Kipping and A. Hill, *J. Chem. Soc.*, **75**, 151 (1899).

ANN ARBOR, MICHIGAN RECEIVED AUGUST 22, 1947

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF MICHIGAN]

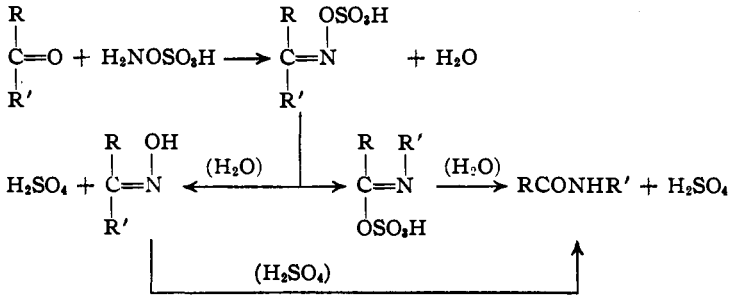
Ketoxime-O-sulfonic Acids[1]

BY PETER A. S. SMITH

Recently,[2] Sanford, Blair, Arroya and Sherk reported on the reaction of hydroxylamine-O-sulfonic acid with ketones, finding that aryl alkyl ketones yield the same amide as obtained from the Beckmann rearrangement of the corresponding oxime, and that aliphatic ketones yield only the oximes. An explanation of these facts was suggested involving the addition of hydroxylamine-O-sulfonic acid to the carbonyl group, subsequent loss of sulfuric acid, and final rearrangement of the organic fragment either to an oxime or to an amide. A different course for this reaction was suggested to the writer by an observation by Sommer, Schulz and Nassau[3] that salts of ketoxime-O-sulfonic acids can be made by the interaction of ketones with neutralized aqueous solutions of hydroxylamine-O-sulfonic acid.

If the initial reaction between a ketone and hydroxylamine-O-sulfonic acid is the elimination of water to form a ketoxime-O-sulfonic acid, then an oxime might arise by hydrolysis of the sulfonyl group, or an amide might arise by direct rearrangement of the sulfonic acid, as indicated below. Some amide might also arise by the Beckmann rearrangement of the oxime under the influence of the sulfuric acid produced by the hydrolysis.

(1) Presented before the Division of Organic Chemistry at the 111th meeting of the American Chemical Society, Atlantic City, April, 1947.
(2) J. K. Sanford, F. T. Blair, J. Arroya and K. W. Sherk, THIS JOURNAL, **67**, 1941 (1945).
(3) F. Sommer, O. F. Schulz and M. Nassau, *Z. anorg. allgem. Chem.*, **147**, 142 (1925).



Continuing our studies[4] on derivatives of hydroxylamine-O-sulfonic acid to investigate this possibility, we have prepared the potassium ketoxime-O-sulfonates of cyclopentanone, cyclohexanone, heptanone-2, acetoacetic ester, phenylacetone, acetophenone, β-acetonaphthone, and α-tetralone. Because of the structural similarity to the O-arylsulfonyl ketoximes, $R_2C{=}NOSO_2Ar$, it was also felt to be of interest to compare the properties of these two classes of compounds.

The potassium ketoxime-O-sulfonates were found to be well-crystallized substances, indefinitely stable when pure and dry. Their solubility in water varies from large to very small, and all are somewhat soluble in boiling alcohol. All were found to oxidize hydriodic acid semiquantitatively, but with varying ease. The salts were caused to decompose by heating, either alone, in the presence of alcoholic alkali, or in the presence of moist or anhydrous hydrogen chloride. The aliphatic ketoxime-O-sulfonates yielded only the oximes when warmed with acid if water was present. In the complete absence of water, the derivatives of heptanone-2, cyclohexanone, and phenylacetone gave rise to basic products, which for the latter two ketones were found to be octahydrophenazine and 2,5-diphenyl-3,6-dimethylpyrazine, respectively; the derivatives of cyclopentanone and acetoacetic ester gave only tars. The aryl alkyl ketoxime-O-sulfonates gave amides in good yield when dry or nearly so, but increasing amounts of water favored hydrolysis to oxime and ketone.

The initial formation of ketoxime-O-sulfonic acids in the reaction of hydroxylamine-O-sulfonic acid with ketones is thus supported by two observations. The structure of the amides obtained from the few unsymmetrical ketones which have been subjected[2] to the reaction corresponds to the configuration of the oxime obtained by treatment of the ketone with hydroxylamine, strongly suggesting that here, too, *cis–trans* isomerism comes into play. That the ketoxime-O-sulfonic acids have the properties required of an intermediate in this reaction is shown by the observations reported in this paper that they can undergo hydrolysis to oximes and rearrangement to amides, and that the relative tendency to follow these respective courses is for different types of ketones the same as that observed in the direct reaction of hydroxylamine-O-sulfonic acid with ketones.

Neber and co-workers[5] have studied the behavior of O-arylsulfonyl ketoximes. These compounds give rise to amides, α-aminoketones, or pyrazines, according to the conditions to which they are exposed. We have found that ketoxime-O-sulfonates decompose to give qualitatively the same products under similar conditions; the reactions are usually not as clean, however. The yields of pyrazines obtained by treating ketoxime-O-sulfonates with alcoholic alkali were considerably lower than those obtained from the arylsulfonyl ketoximes. The ketoxime-O-sulfonates might nevertheless be useful for preparing pyrazines in cases where the corresponding arylsulfonyl ketoximes are too unstable to be handled easily; the isolation of some of the latter compounds is rendered inconvenient by the ease with which they deflagrate.

The mechanism by which pyrazines arise in the decomposition of ketoxime-O-sulfonates is not entirely clear, but is presumably similar to that which has been elucidated for the analogous reaction of arylsulfonylketoximes.[5] No evidence for the formation of a pyrazine from cyclopentanoxime-O-sulfonic acid could be obtained, which is reminiscent of the reported failure of α-chlorocyclopentanone to yield a pyrazine when treated with alcoholic ammonia,[6] although α-chlorocyclohexanone gave octahydrophenazine in 25% yield under this treatment.

Experimental

The potassium ketoxime-O-sulfonates were prepared by adding one-tenth equivalent of potassium carbonate or acetate in concentrated aqueous solution to an aqueous or methanolic solution of one-tenth equivalent each of hydroxylamine-O-sulfonic acid and ketone in an ice-bath. It is necessary first to allow sufficient time, usually about one minute, for the latter two reagents to react, as evidenced by the formation of a homogeneous solution. If this is not done, potassium hydroxylamine-O-sulfonate is obtained, which deflagrates with violence during subsequent operations. The desired salts crystallized on scratching, and were filtered and washed with water and/or methanol, followed by ether or benzene. Those salts which are appreciably soluble in water could not be freed of potassium sulfate by washing. Where purification could not be accomplished by recrystallization from water or alcohol, advantage was taken of the fact that potassium ketoxime-O-sulfonates as first formed are in highly supersaturated solution, but the contaminating potassium sulfate is present as a suspension in the alcoholic solution. Rapid filtration at this stage through a bed of Filter-Cel accomplished the desired purification. For the recrystallizations, it was found best to filter the hot solutions through

(4) R. N. Keller and P. A. S. Smith, THIS JOURNAL, 68, 899 (1946).

(5) P. W. Neber and A. Friedolsheim *Ann.*, 449, 109 (1926); P. W. Neber and H. Uber, *Ann.*, 467, 52 (1928); P. W. Neber and A. Burgard, *Ann.*, 493, 281 (1932); P. W. Neber and G. Huh, *Ann.*, 515, 283 (1935); P. W. Neber, A. Burgard and W. Thier, *Ann.*, 526, 277 (1936).

(6) M. Godchot and M. Mousseron, *Bul. soc. chim.*, [4] 51, 360 (1932).

TABLE I

PROPERTIES OF POTASSIUM KETOXIME-O-SULFONATES

Parent ketone	Formula of sulfonate	K_2SO_4, % Calcd.	Found	Iod. eq. wt. Calcd.	Found	M. p., °C.	Yield, %	Solubility H_2O	EtOH	Prod. from dry HCl treatment
Heptanone-2[a]	$C_7H_{14}O_4NSK$	35.20	36.05	123.5	139	180–185	55	v. s.	s. s.	Unident. basic oil b. p. 245° (735 mm.)
Acetoacetic ester[b]	$C_6H_{10}O_6NSK$	33.10	33.32	167.5	151	164–166	55	s.	i.	Unident. dark oil
Cyclopentanone[b]	$C_5H_8O_4NSK$	40.05	40.65	108.7	111	169 dec.	56	s.	i.	Tar[c]
Cyclohexanone[a,b]	$C_6H_{10}O_4NSK$	37.68	37.07	115.7	120	d. 155–180	52	s. s.	s. s.	Octahydrophenazine; m. p. 108–109°, >7%[d]
Phenylacetone[e]	$C_8H_{10}O_4NSK$	32.55	32.75	133.5	123	170–185	theo. 2	s. s.	i.	2,5-DiPh-3,6-di-Me-pyrazine, 14%[e]
Acetophenone[a,b]	$C_8H_8O_4NSK$	34.38	33.75			215–220	47	s.	s. s.	Acetanilide, 77%[f]
β-Acetonaphthone[a]	$C_{12}H_{10}O_4NSK$	29.70	29.35	151.7	145	205–210	40	i.	i.	β-Acetnaphthalide, m. p. 132–133°, 87%[g]
α-Tetralone[a]	$C_{10}H_{10}O_4NSK$	31.18	31.45	139.5	158	173–175	67	v. s.	i.	Largely α-tetralone, + <12% α-naphthylamine[h]

[a] Prepared from potassium acetate. [b] Prepared from potassium carbonate. [c] In the presence of moisture, cyclopentanoxime, 55%. [d] In the presence of moisture, cyclohexanoxime, 89%. When treated with alc. NaOH, only unident. oils produced. [e] When treated with alc. NaOH at T. > 40°, and worked up after Neber's[6] directions for *p*-tolylphenylacetoxime, there was produced 56% of 2,5-di-Ph-3,6-di-Me-pyrazine, m. p. 125–128°, or 22% of the acetate of 1-phenyl-1-aminoacetone diethyl acetal, m. p. 145–147°. [f] In the presence of moisture, 36% of acetophenoxime plus a smaller amount of acetanilide plus a little acetophenone. The dry salt heated alone gave 47% of acetanilide, m. p. 112–114°. [g] In the presence of several equivs. of water, β-acetonaphthoxime, 85%, plus a little β-acetonaphthone. [h] When heated in dry pyridine, a little dihydrohomocarbostyryl, m. p. 143–144°, was formed. When heated with alc. NaOH, only dark, non-basic oils were formed.

a preheated, sintered-glass filter with the aid of compressed air, because of the sharp temperature gradient of the solubilities in the neighborhood of the boiling point. Yields on recrystallization were generally about 50–60%.

The hydroxylamine-O-sulfonic acid was prepared from hydroxylamine sulfate and chlorosulfonic acid.[3] α-Chlorocyclohexanone was obtained from Farchan Laboratories; heptanone-2, phenylacetone, α-tetralone, and cyclohexanoxime were prepared by standard procedures; and the remainder of the organic chemicals used were Eastman Kodak Co. products.

The potassium ketoxime-O-sulfonates were analyzed for potassium by fuming to dryness with sulfuric acid, and in addition were titrated iodometrically. The equivalent weights given by the latter determination are subject to an error of as much as 10%, because of the long time, usually about forty-eight hours, required for complete reaction with the iodide.

In the accompanying table are listed the principal properties of the potassium ketoxime-O-sulfonates prepared.

Rearrangement of Ketoxime-O-sulfonates.—Approximately 4 *N* solutions of hydrogen chloride in dioxane were prepared from tank hydrogen chloride dried successively over sulfuric acid and phosphorus pentoxide, and dioxane freshly distilled from sodium. Mixtures of the ketoxime-O-sulfonates and several equivalents of the acid solutions were heated near the boiling point for periods of from ten minutes to an hour, after which they were treated with water and worked up for the neutral, acidic and basic components. The products obtained are listed in the accompanying table; products obtained from other ways of decomposing the compounds are described in footnotes to the table.

Octahydrophenazine.—The product, m. p. 108–109°, which was extracted with some difficulty from the tars obtained as above from potassium cyclohexanoxime-O-sulfonate was identified with the octahydrophenazine, m.p. 107–108°, obtained in 25% yield by Godchot and Mousseron[6] by the action of ammonia on α-chlorocyclohexanone. Because these authors neglected to publish analytical data either for octahydrophenazine or its picrate, we repeated their preparation. The product was obtained in 37% yield using a six-day reaction time and a rapid addition of ammonia; separation of the product from tar was facilitated by precipitation from the acidified reaction mixture with ammonia instead of alkali, and recrystallizing alternately from acetone and petroleum ether, in which the tar is respectively very soluble and almost insoluble. *Anal.*[7] Calcd. for $C_{12}H_{16}N_2$: C, 76.60; H, 8.58; N, 14.92, mol. wt., 188. Found: C, 76.60; H, 8.55; N, 14.65; mol. wt. (ebullioscopic in benzene[8]), 192, 193.

A picrate was obtained as yellow prisms from ethanol; m.p. 162–163°. *Anal.*[7] Calcd. for $C_{12}H_{16}N_2 \cdot 2C_6H_3O_7N_3$: C, 44.60; H, 3.42; N, 17.35. Found: C, 44.58; H, 3.55; N, 16.83, 16.77. Godchot and Mousseron reported m.p. 163–164° for a "monopicrate" for which they gave no analysis.

A chloroaurate was obtained as tiny yellow needles from water; m.p. 145–146° after recrystallization from absolute ethanol. *Anal.*[7] Calcd. for $C_{12}H_{16}N_2 \cdot HAuCl_4 \cdot C_2H_5OH$: C, 29.28; H, 4.04; Au, 34.4. Found: C, 28.55; H, 4.14; Au, 36.05. No formulation for this compound which gives a more satisfactory agreement with the analytical data is immediately apparent.

Because of the singular reactions by which octahydrophenazine is formed, it was felt desirable to confirm its structure. An attempt to dehydrogenate it to phenazine by means of iodine in acetic acid[9] gave only an insoluble, black resin. But oxidation of 0.19 g. with potassium permanganate in alkaline solution gave 0.035 g., 14%, of a water-soluble, amphoteric solid, identified by its m.p. of 206–208° and the red-violet color given with ferrous sulfate solution as the expected pyrazine-2,3,5,6-tetracarboxylic acid.[10]

***p*-Toluenesulfonylcyclohexanoxime.**—A solution of 9.5 g. of *p*-toluenesulfonyl chloride in 15 cc. of pyridine was added dropwise with stirring to one of 5.6 g. of cyclohexanoxime in 10 cc. of pyridine in an ice–methanol-bath. The mixture was kept at 0° for four hours and then poured

(7) Analyses for C, H, N and Au by Micro-Tech Laboratories, Skokie, Ill.

(8) A. W. C. Menzies, THIS JOURNAL, 43, 2309 (1921).

(9) G. R. Clemo and H. McIlwain, *J. Chem. Soc.*, 1993 (1934).

(10) L. Wolff, *Ber.*, 26, 722 (1893).

on a slurry of ice and dilute sulfuric acid. The oil which separated in large amount crystallized in a few seconds, but upon warming to room temperature during filtration and washing, it deflagrated vigorously. In subsequent preparations, it was therefore taken up in cold benzene and dried and handled in that solvent. Treatment of such a benzene solution with hydrogen chloride in dioxane gave no crystallizable product. Treatment with alcoholic sodium hydroxide yielded less than 5% of octahydrophenazine. *p*-Toluenesulfonylphenylacetoxime likewise gave no crystalline products when treated with hydrogen chloride in dioxane.

Summary

1. The potassium oxime-O-sulfonates of eight ketones have been prepared.

2. Aqueous acid hydrolyzes these compounds to the corresponding oximes; anhydrous hydrogen chloride converts aryl alkyl ketoxime-O-sulfonates to amides by a Beckmann-type rearrangement, and converts some dialkyl ketoxime-O-sulfonates to pyrazines in low yield.

3. These reactions are related to the direct reaction of hydroxylamine-O-sulfonic acid with ketones, and to the reactions of O-arylsulfonyl ketoximes.

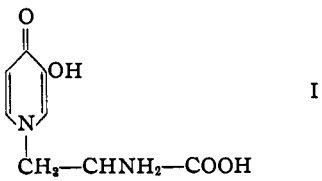
ANN ARBOR, MICH. RECEIVED SEPTEMBER 8, 1947

[CONTRIBUTION FROM THE DEPARTMENT OF RESEARCH IN PURE CHEMISTRY, MELLON INSTITUTE]

On the Structure of Leucaenine (Leucaenol) from *Leucaena Glauca* Bentham. III

BY A. F. BICKEL[1]

According to the experimental evidence now available, the most probable structure of leucaenine, an amino acid occurring in the tropical plant, *Leucaena glauca* Bentham, is β-[N-(3-hydroxypyridone-4)]-α-aminopropionic acid (I). The formation of 3,4-dihydroxypyridine on pyrolysis[2,3,4] and of N-methyl-3-methoxy-pyridone-4 on degradative methylation[5,6,7] proved the presence of a 3,4-dihydroxypyridine ring in leucaenine. These two reactions made it very probable that the part of the molecule containing the amino-acid residue is *not* bound to one of the carbon atoms of the pyridine ring. Since leucaenine is not split by treatment with 48% hydrobromic acid,[2] the alanine side-chain can*not* be bound to one of the hydroxyl groups of the ring. Hence, structure I was assumed to be the most probable.



I

The object of the present investigation was to attempt to provide definite proof of the existence of an alanine side-chain and to demonstrate its position in the molecule. It is known that a compound of a structure comparable to that of leucaenine, N-methyl-3-hydroxypyridone-4, yields methylamine[5] on oxidation with potassium permanganate. Should the oxidation of leucaenine proceed in the same way, formation of α,β-diaminopropionic acid may be expected. This diamino acid is, however, oxidized by potassium permanganate. Thus it was imperative to find an oxidizing agent capable of breaking the ring, while leaving the diamino acid unattacked. An aqueous solution of bromine proved to be a suitable reagent; hence the reaction of leucaenine with this oxidizing agent has been investigated more closely.

Upon oxidation of an aqueous suspension of leucaenine with bromine, a small amount of a compound $C_3H_9O_2N_2Br$ is formed. The specific rotation is $[\alpha]^{27}D$ +13° (33 mg. dissolved in 5 cc. of 0.37% hydrochloric acid). Aqueous solutions of this substance as well as of *dl*-α,β-diaminopropionic acid hydrobromide, prepared by synthesis, show an acid reaction (*p*H of the saturated solution in both cases, 4), react with an acidified aqueous solution of silver nitrate to yield silver bromide, and show a strong ninhydrin reaction. On heating in a melting point capillary, both compounds (as well as their mixture) gradually turn brown above 200° and melt above 236° with decomposition.

Geiger counter spectrometer diffraction patterns of the two substances were prepared with CuKα radiation. These patterns both show a large number of sharp diffraction lines, identical in positions and intensities in both cases.

Ultraviolet absorption spectra of aqueous solutions were found to be essentially the same for both compounds; they showed gradually increasing absorption with decreasing wave length, but no characteristic maxima.[8] The shape of the curves obtained closely resembles that found by Ley and Vanheiden[9] for *dl*-α,β-diaminopropionic acid hydrochloride.

The above facts clearly prove that the substance isolated is α,β-diaminopropionic acid hydrobro-

(1) Visiting Fellow, Netherland-America Foundation.

(2) Adams, Cristol, Anderson and Albert, THIS JOURNAL, 67, 89 (1945).

(3) Bickel, *ibid.*, 69, 1805 (1947).

(4) Adams, Jones and Johnson, *ibid.*, 69, 1810 (1947).

(5) Bickel and Wibaut, *Rec. trav. chim.*, 65, 65 (1946).

(6) Wibaut and Kleipool, *ibid.*, 66, 24 (1947).

(7) Bickel, THIS JOURNAL, 69, 1801 (1947).

(8) The author is indebted to Dr. Harold P. Klug, Dr. Alfred L. Marston and Mr. Joseph H. Lieblich, all of the Department of Research in Chemical Physics at Mellon Institute, for carrying out the physical determinations.

(9) Ley and Vanheiden, *Z. anorg. allgem. Chem.*, 188, 251 (1930).